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EXAMINER	
EWOLDT, GERALD R	
ART UNIT	**PAPER NUMBER**
1644	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/634,309	DOTAN ET AL.	
	Examiner	Art Unit	
	G. R. Ewoldt, Ph.D.	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 October 2006 and 17 January 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☐ Claim(s) *1-59* is/are pending in the application.

4a) Of the above claim(s) *21 and 46-59* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-20 and 22-45* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's election of Group I in the paper filed 5/10/06, has been previously acknowledged. Because Applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)). Applicant's election of the antibody species: a **combination** of anti-Glc(α1-4)Glc(α) and anti-Glc(α) and anti-GlcNAc(α) and anti-L-Rha(α) is also acknowledged. Applicant's further election of the antibody isotype: IgM is also acknowledged. Upon reconsideration the antibody isotype species election requirement has been withdrawn.

NOTE: The claims were originally examined as reciting a method employing only the elected species of antibodies, i.e., a combination of the four antibody species. A method employing the elected antibody species, a **combination** of anti-Glc(α1-4)Glc(α) and anti-Glc(α) and anti-GlcNAc(α) and anti-L-Rha(α) is free of the art. Accordingly the search was extended to include a method employing an anti-Glc(α1-4)Glc(α) and an anti-GlcNAc antibody. Said method is also free of the prior art.

2. Claims 46-59 stand withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to non-elected inventions. Claim 21 is withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected species.

Claims 1-20 and 22-45 are being acted upon.

3. In view of Applicant's amendments and remarks, filed 10/25/06 and 1/17/07, the previous rejections under the second paragraph of 35 U.S.C. 112 A), B), and D), as well as the rejection for omitting essential steps, have been withdrawn. Additionally, the rejection under 35 U.S.C. 102(b) has also been withdrawn.

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claim 16 stands rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, specifically:

C) Claim 16 is vague and indefinite as it is unclear what is encompassed by "an early diagnosis" of MS.

Applicant's arguments, filed 10/25/06, have been fully considered but they are not persuasive. Applicant cites three references in support of the term.

A review of the references, Exhibits A-C, reveals that in none of them is the term, "an early diagnosis" of MS, defined. Indeed, in the context of Exhibit C, Whitney, D.K. (2001), it appears that the author is using the term to imply MS that is diagnosed by a primary care provider, whereas in the other Exhibits there is no indication of the this limitation.

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 1-20 and 22-45 stand rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Specifically, the specification provides insufficient evidence that the method of the instant claims would function as claimed.

As set forth previously, A review of the specification discloses that the method of the instant claims presumably functions through a measurement of certain antibody levels in a subject as compared to a control wherein a higher level of certain antibodies in a subject is indicative of MS.

A review of the specification discloses that the claimed method cannot function as broadly claimed. See for example page 18 wherein it is disclosed that the method works only in with IgM, i.e., no significant difference were found in studies of IgG or IgA levels. For this reason alone the claimed method must be considered to be unpredictable and requiring of undue experimentation. A further review of the Inventor's own work raises additional issues. See, for example Schwarz et al. 2006. Therein the Inventor's teach a number of embodiments wherein the claimed method would not diagnose or predict MS. For example, while certain

antibodies might distinguish an MS patient from a healthy patient, the authors established that anti-Glc(α), anti-GlcNAc(α), and anti-Rha(α) antibodies could not distinguish MS patients from patients with other autoimmune diseases. And no difference in antibody levels were found that could be used to distinguish treated from untreated MS patients. This finding, along with the finding that levels of most antibodies are not significantly different in patients with the less severe RRMS and the more severe PPMS, would argue that the claimed method could also not effectively distinguish, exacerbation of disease (Claim 22), remission of disease (Claim 26), nor severity of disease (Claim 36). Accordingly, given the breadth of the claims and the state of the art, the method of the instant claims must be considered unpredictable and requiring of undue experimentation.

Applicant's arguments, filed 10/25/06, have been fully considered but they are not persuasive. Applicant argues that the claims have been limited to the specific antibody isotypes that have been shown in the specification to correlate with disease status.

It is unclear where in the specification said showing referred to by Applicant is to be found.

Applicant argues that Schwarz et al. 2006 actually supports the claimed invention citing a statistical tendency in Exhibit G.

As set forth in the rejection, Schwarz et al. 2006 established that anti-Glc(α), anti-GlcNAc(α), and anti-Rha(α) antibodies could **not** distinguish MS patients from patients with other autoimmune diseases. Applicant has not addressed this issue. Further, the bulk of reference details work employing only anti-Glc(α1-4)Glc(α) antibodies. Regarding Exhibit G, data presented out of context outside of an executed declaration cannot be considered to be persuasive.

Applicant cites Example 3 in support of Claims 22-35 and 37-45.

First note that the Examiner's copy of the specification includes no Example 3. The Examples are numbered 1, 2, 4, and 8-10. Regardless, the disclosures of the specification are not commensurate in scope with the breadth of the claims. For example, the disclosure of Example 2 refers **only** to results employing anti-Glc(α) and anti-Glc(α1-4)Glc(α) antibodies.

Applicant admits that, "Schwarz reported that no significant difference in the level of all four anti-glycan IgM antibodies was found between treated and untreated RRMS patient

groups, or between RRMS patients at relapse or remission," but concludes that, "these findings do not compel a conclusion that these antibody levels cannot be used to predict relapse or to monitor the effectiveness of treatment. These types of assessment can only be performed in studies designed for this purpose such as controlled prospective studies designed with continual follow-up patients, and using samples from untreated patients at the early stages of the diseases."

The findings of the reference, as well as Applicant's argument, do compel a conclusion that the invention of the instant claims at most comprises only an idea for further study and not a patentable invention.

Applicant cites Exhibits D-F.

Exhibit D employed only an anti-Glc(α1-4)Glc(α) antibody and only in the context of predicting CIS. Said context and prediction is not disclosed in the specification and regardless, is not commensurate in scope with the breadth of the claimed invention.

Exhibit E studied post CIS patients, again this is not a patient population disclosed in the specification nor recited in the claims. Further, while the anti-Glc(α1-4)Glc(α) antibody of the reference is one of the antibodies recited for use in the claimed method, the anti-Glc(α1-6)Glc(α) antibody is not. It is also noted that while apparently tested, the results did **not** find that the anti-GlcNAc antibody correlated with conversion of CIS to RRMS.

Exhibit F again employed only the anti-Glc(α1-4)Glc(α) antibody and again only in the context of conversion of CIS to RRMS.

Thus, it is apparent that while the anti-Glc(α1-4)Glc(α) antibody has been fairly well studied in the context of conversion of CIS to RRMS, it is also apparent the majority of the antibodies recited in the claimed method have not been studied and even the anti-Glc(α1-4)Glc(α) antibody has not been studied in all of the claimed contexts.

8. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or

improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

9. Claims 1-20 and 22-45 stand rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over Claims 1-20 and 22-45 of U.S. Application No. 10/835,607. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of the '607 application recite the same method but not the same elected species (as no species restriction has yet been set forth).

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

10. Claims 1-20 and 22-45 stand rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over Claims 1-20 and 22-45 of U.S. Application No. 11/047,124. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of the '124 application recite the same method but not the same elected species (as no species restriction has yet been set forth).

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Applicant indicates that the double patenting rejections

will be addressed upon the finding of allowable subject matter.

11. No claim is allowed.

12. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Dr. Gerald Ewoldt whose telephone number is (571) 272-0843. The examiner can normally be reached Monday through Thursday from 7:30 am to 5:30 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841.

13. **Please Note**: Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197.

10/26/07

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